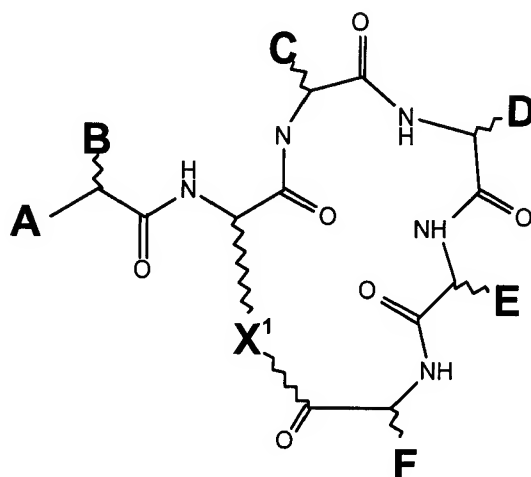


1. **AMENDMENT TO THE CLAIMS (LISTING OF CLAIMS):**

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Previously Presented) A method of treatment of osteoarthritis, comprising the step of administering an effective amount of an inhibitor of a C5a G protein-coupled receptor to a subject in need of such treatment, in which the inhibitor is a compound which
 - (a) is an antagonist of a C5a G protein-coupled receptor,
 - (b) has substantially no agonist activity, and
 - (c) is a cyclic peptide or peptidomimetic compound of formula-I:



(I)

where **A** is H, alkyl, aryl, NH₂, NH-alkyl, N(alkyl)₂, NH-aryl, NH-acyl, NH-benzoyl, NHSO₃, NHSO₂-alkyl, NHSO₂-aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or **B** is the side chain of L-phenylalanine or L-phenylglycine;

C is the side chain of glycine, alanine, leucine, valine, proline, hydroxyproline, or thioproline;

D is the side chain of D-leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine;

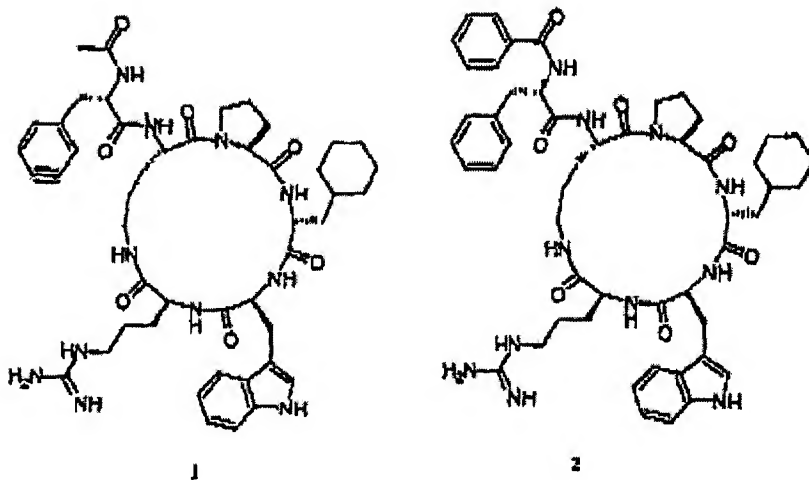
E is the side chain of an amino acid selected from the group consisting of L-phenylalanine, L-tryptophan and L-homotryptophan, or is L-1-naphthyl or L-3-benzothienyl alanine;

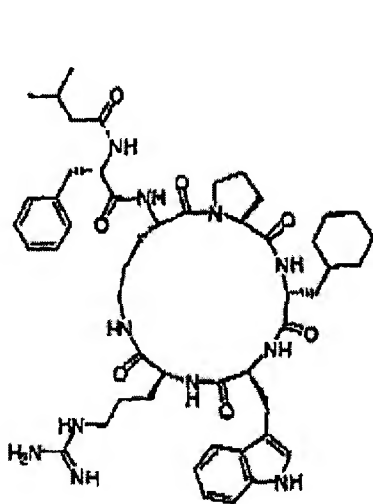
F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

X¹ is -(CH₂)_nNH- or (CH₂)_nS-, where *n* is an integer of from 1 to 4; -(CH₂)₂O-; -(CH₂)₃O-; -(CH₂)₃-; -(CH₂)₄-; -CH₂COCHRNH-; or -CH₂-CHCOCHRNH-, where R is the side chain of any common or uncommon amino acid.

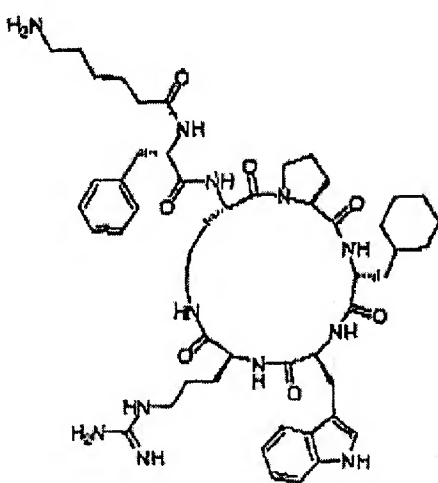
2. (Previously Presented) The method of claim 1, in which n is 2 or 3.
3. (Withdrawn) The method of claim 1, in which **A** is an acetamide group, an aminomethyl group, or a substituted or unsubstituted sulphonamide group.
4. (Withdrawn) The method of claim 2, in which **A** is a substituted sulphonamide, and the substituent is an alkyl chain of 1 to 6 carbon atoms, or a phenyl or toluyl group.
5. (Withdrawn) The method of claim 3, in which the substituent is an alkyl chain of 1 to 4 carbon atoms.
- 6.-9. (Canceled)
10. (Previously Presented) The method of claim 1, in which the inhibitor is a compound which has antagonist activity against C5aR, and has no C5a agonist activity.

11. (Previously Presented) The method of claim 1, in which the inhibitor has potent antagonist activity at sub-micromolar concentrations.
12. (Previously Presented) The method of claim 1, in which the compound has a receptor affinity $IC_{50} < 25 \mu M$, and an antagonist potency $IC_{50} < 1 \mu M$.
13. (Currently Amended) The method of claim 1, in which the compound is selected from the group consisting of: compounds 1 to 6, 10 to 15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33 to 37, 39 to 45, 56 to 58 and 60 to 64, wherein said compounds have chemical structures as follows:

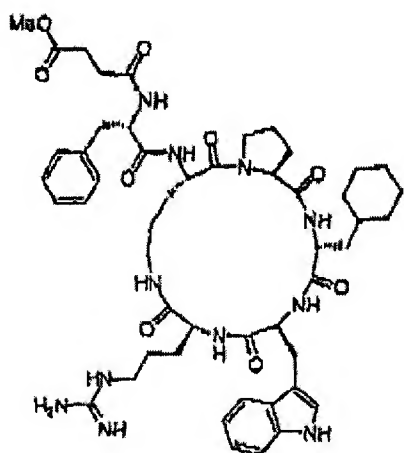




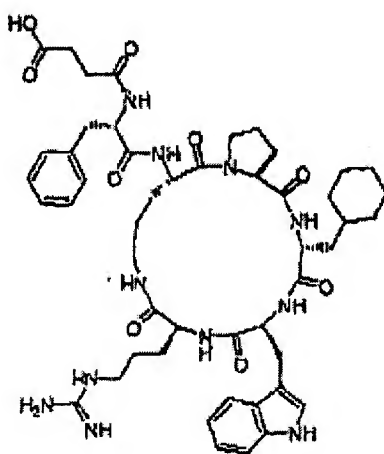
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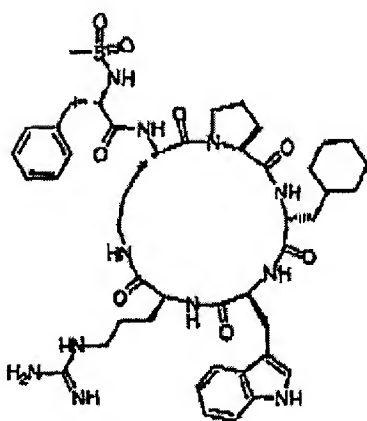
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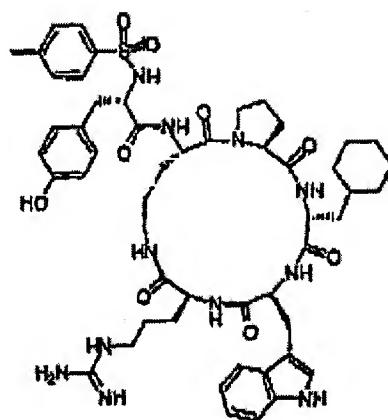
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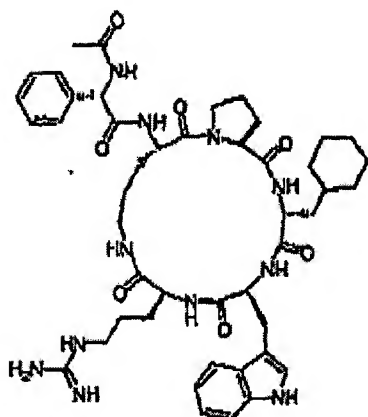
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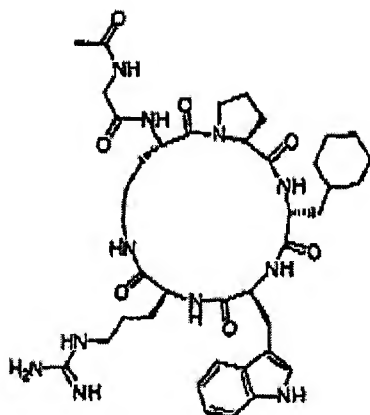
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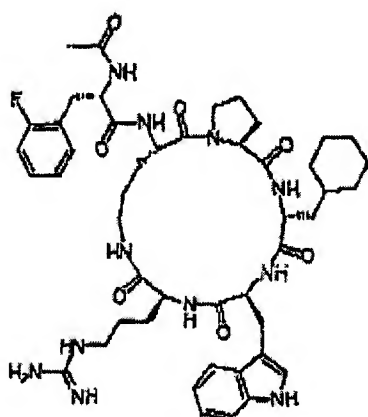
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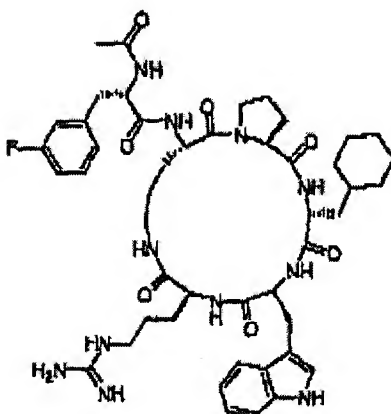
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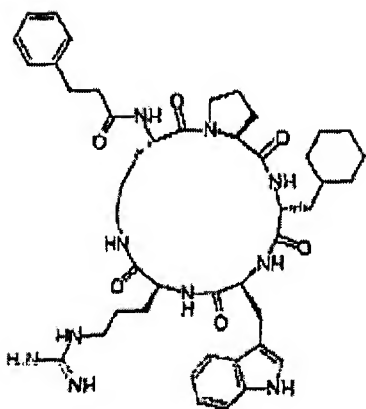
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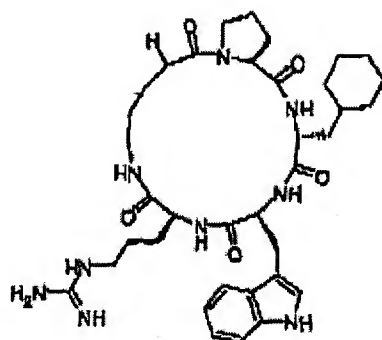
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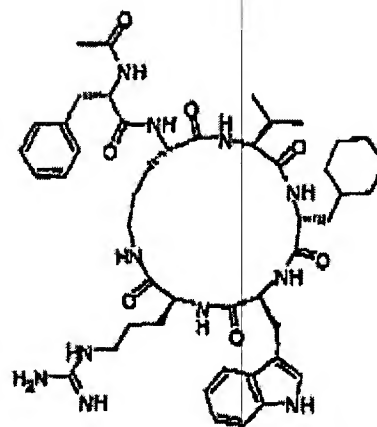
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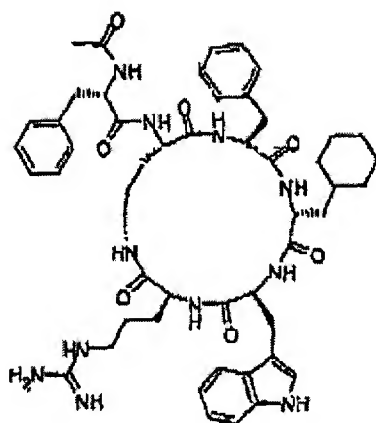
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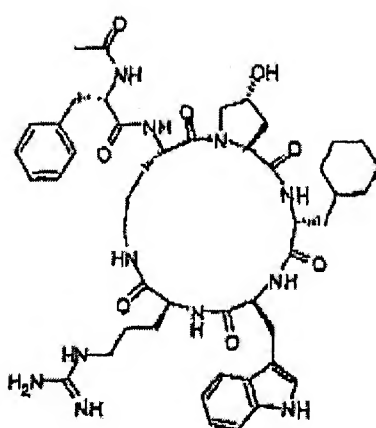
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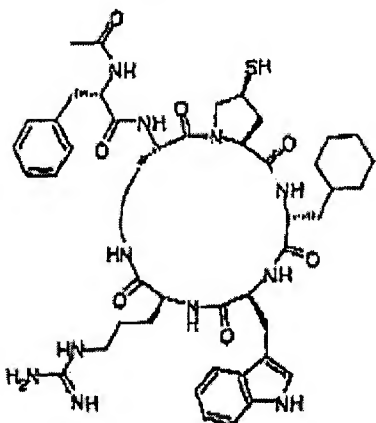
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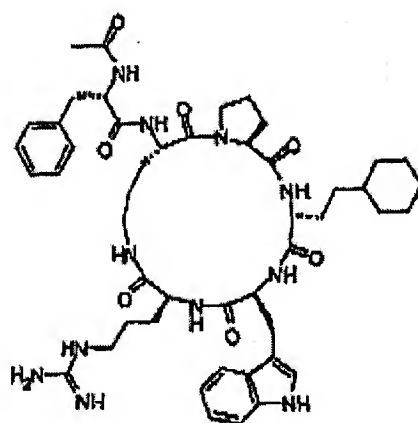
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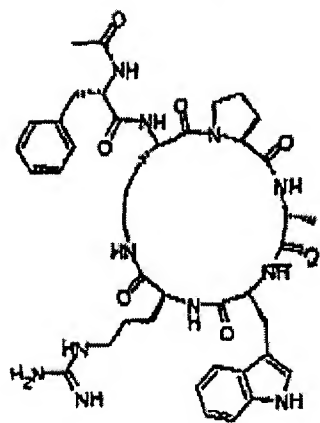
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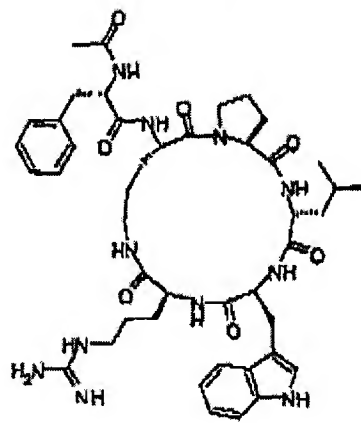
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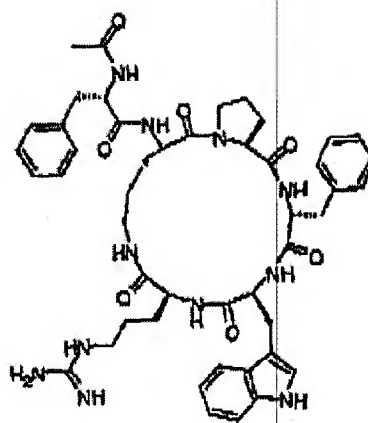
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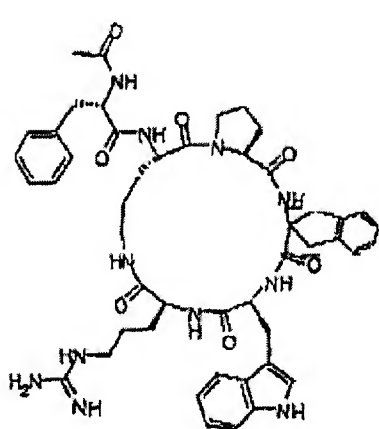
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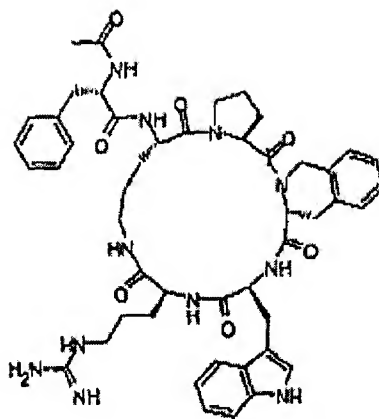
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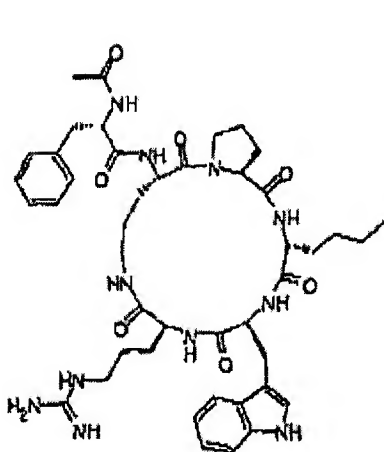
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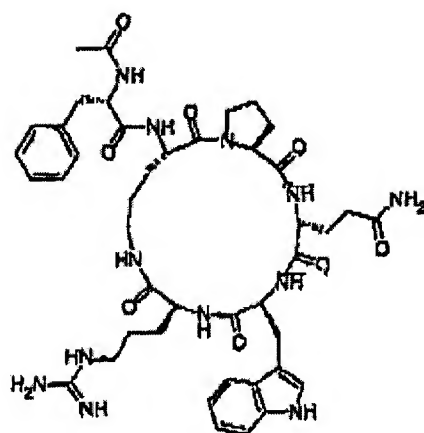
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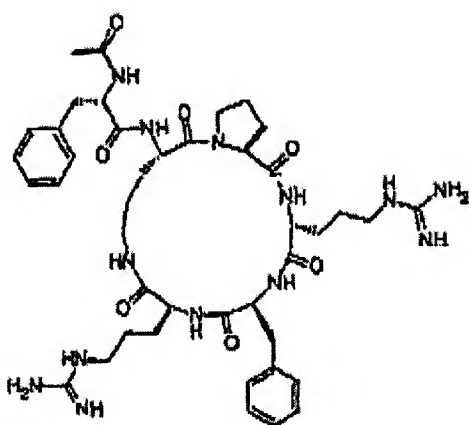
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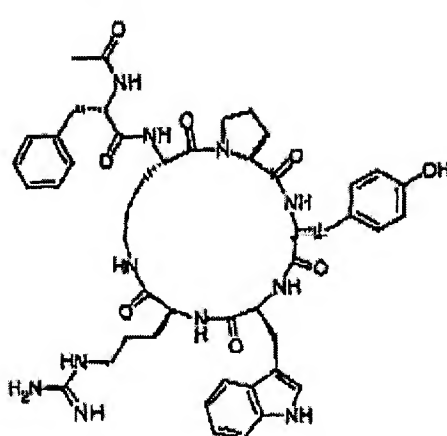
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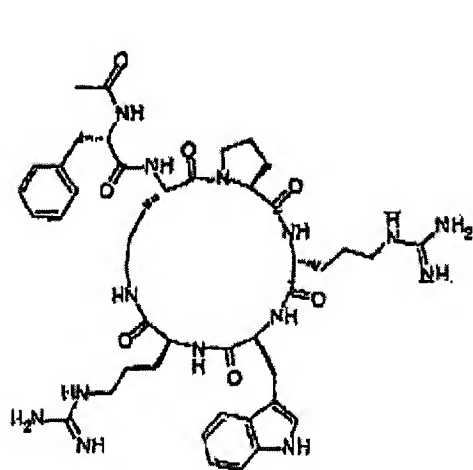
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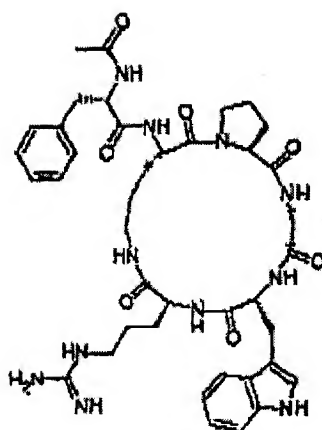
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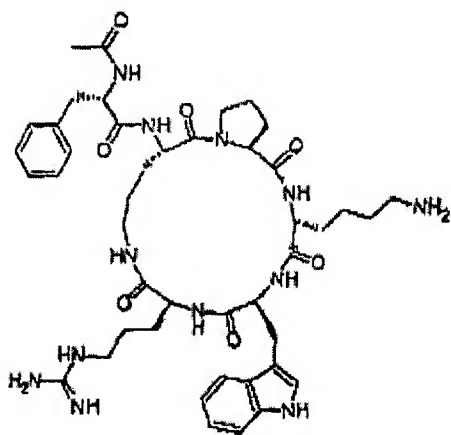
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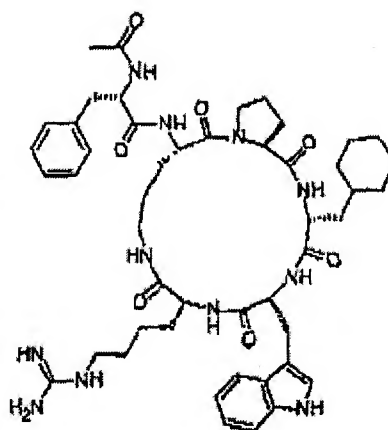
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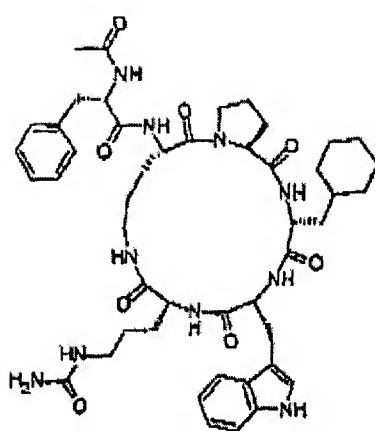
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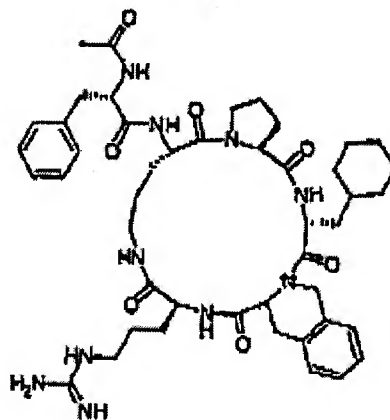
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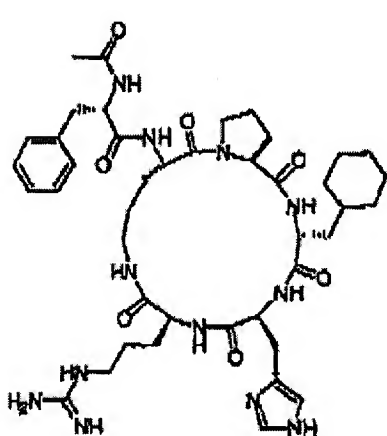
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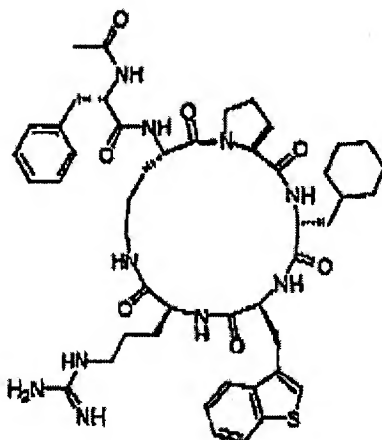
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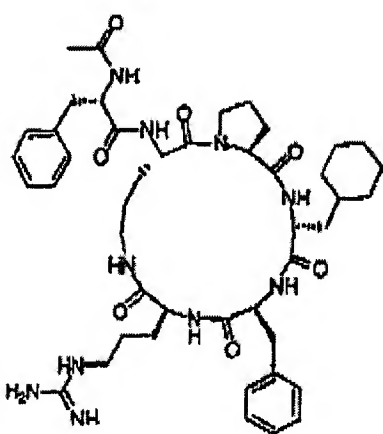
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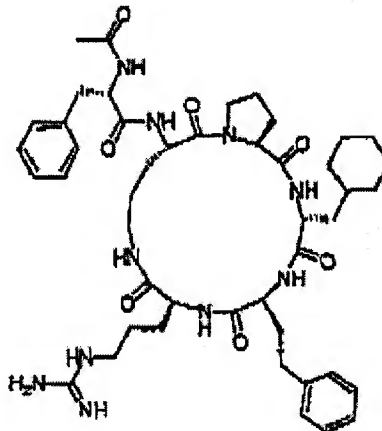
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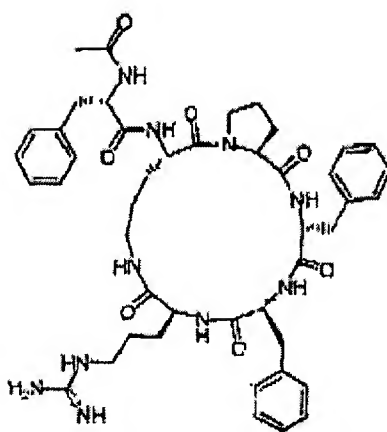
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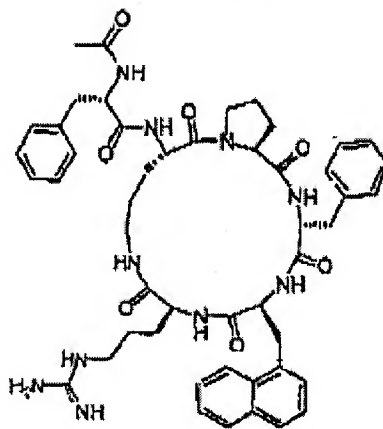
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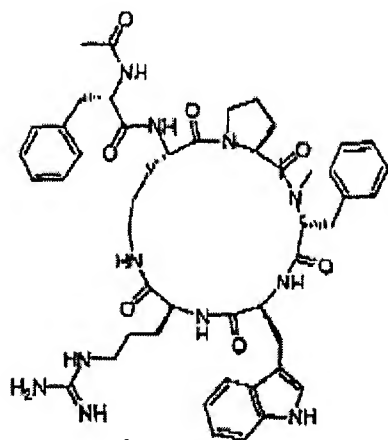
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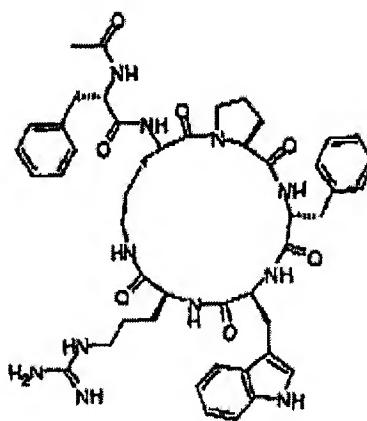
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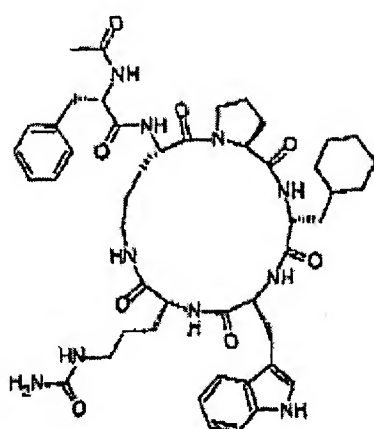
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- The image shows the chemical structure of a cyclic peptide. It consists of a central ring representing the peptide backbone, with several side chains attached. The side chains include a benzyl group, a cyclohexyl group, a tryptophan residue (indole ring), and a guanidinoethyl group. The structure is drawn in a circular fashion, with the backbone forming a continuous loop.

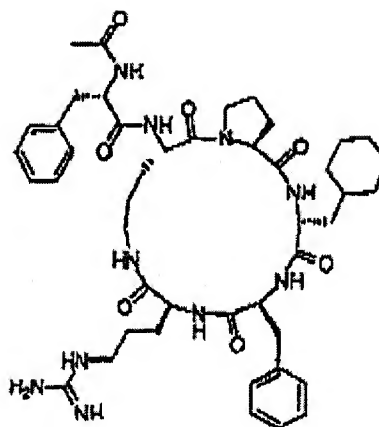
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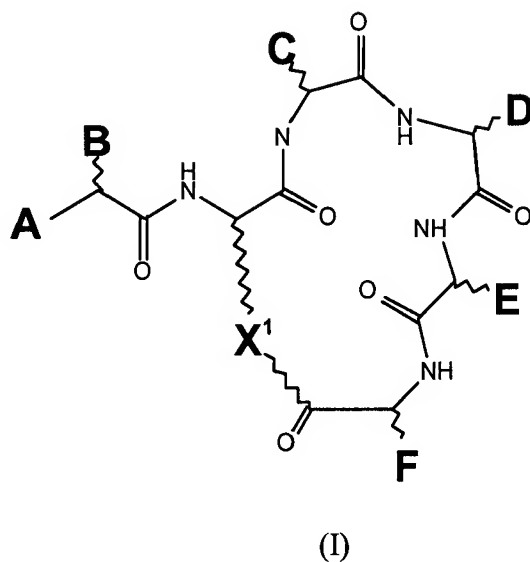
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15. (Previously Presented) The method of claim 1, in which the inhibitor is used in conjunction with one or more other agents for the treatment of osteoarthritis.
16. (Previously Presented) The method of claim 1, wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and **X¹** is $-(CH_2)_nNH-$, where n is 3.
17. (Previously Presented) A method for treating osteoarthritis in a mammal, said method comprising the step of: administering to a mammal in need thereof, an effective amount of a composition comprising a C5a G protein-coupled receptor antagonist compound that

(a) has substantially no agonist activity and (b) is a cyclic peptide or peptidomimetic compound of formula I:



wherein:

A is H, alkyl, aryl, NH₂, NH-alkyl, N(alkyl)₂, NH-aryl, NH-acyl, NH-benzoyl, NHSO₃, NHSO₂-alkyl, NHSO₂-aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or **B** is the side chain of L-phenylalanine or L-phenylglycine;

C is the side chain of glycine, alanine, leucine, valine, proline, hydroxyproline, or thioproline;

D is the side chain of D-leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine;

E is the side chain of an amino acid selected from the group consisting of L-phenylalanine, L-tryptophan and L-homotryptophan, or is L-1-naphthyl or L-3-benzothienyl alanine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

X¹ is $-(CH_2)_nNH-$ or $(CH_2)_nS-$, where n is an integer of from 1 to 4; $-(CH_2)_2O-$; $-(CH_2)_3O-$; $-(CH_2)_3-$; $-(CH_2)_4-$; $-CH_2COCHRNH-$; or $-CH_2-CHCOCHRNH-$, where R is the side chain of any common or uncommon amino acid.

18. (Currently Amended) The method of claim 17, wherein

A is H, alkyl, aryl, NH_2 , NH-alkyl, $N(alkyl)_2$, NH-aryl, NH-acyl, NH-benzoyl, $NHSO_3$, $NHSO_2$ -alkyl, $NHSO_2$ -aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or **B** is the side chain of L-phenylalanine or L-phenylglycine;

C is the side chain of glycine, alanine, leucine, valine, proline, hydroxyproline, or thioproline;

D is the side chain of D-leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine;

E is the side chain of an amino acid selected from the group consisting of L-phenylalanine, L-tryptophan and L-homotryptophan, or is L-1-naphthyl or L-3-benzothienyl alanine;

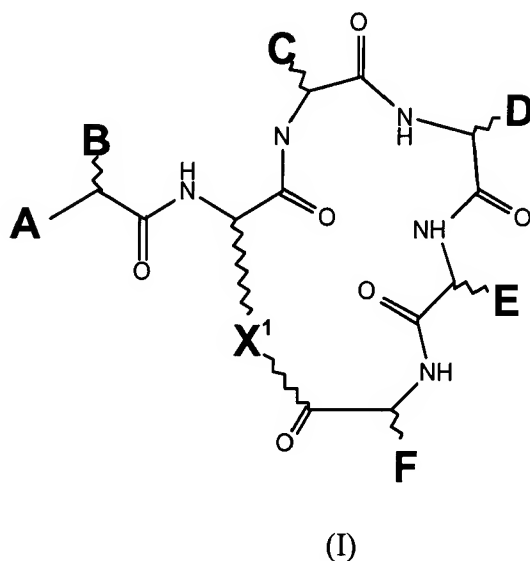
F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine; and

X¹ is $-(CH_2)_nNH-$ or $(CH_2)_nS-$, where n is an integer from 1 to 4.

19. (Previously Presented) The method of claim 18, wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and **X¹** is $-(CH_2)_nNH-$, where n is 3.

20. (Previously Presented) A method of treatment of osteoarthritis, said method comprising the step of administering to a subject in need thereof, an effective amount of a pharmaceutically-acceptable composition that comprises a C5a G protein-coupled receptor inhibitor, wherein said inhibitor:

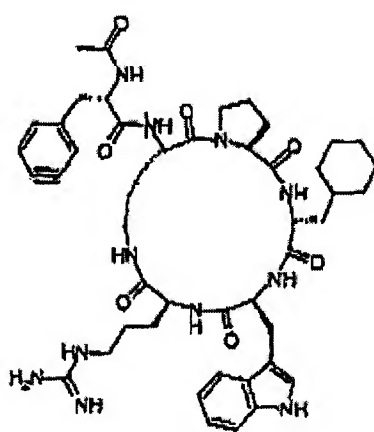
- (a) is an antagonist of a C5a G protein-coupled receptor;
- (b) has substantially no agonist activity; and
- (c) is a cyclic peptide or peptidomimetic compound of formula I:



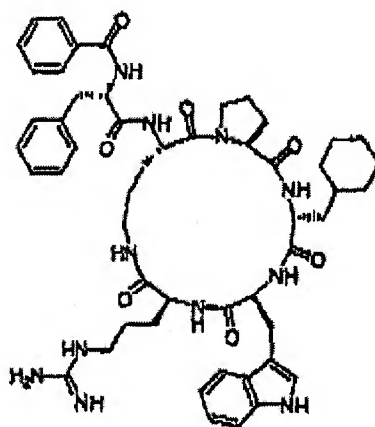
wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the

side chain of L-tryptophan; F is the side chain of L-arginine; and X^1 is $-(CH_2)_nNH-$, where n is 3.

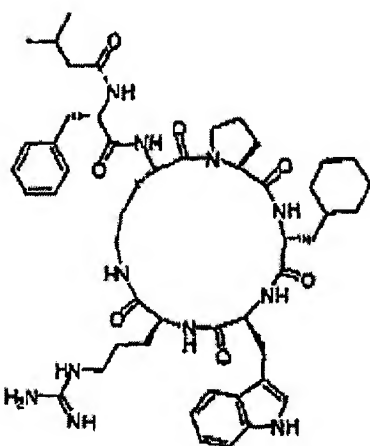
21. (Previously Presented) A method of treating osteoarthritis in a subject, said method comprising the step of administering to said subject an effective amount of a cyclic peptide or peptidomimetic compound selected from the group consisting of:



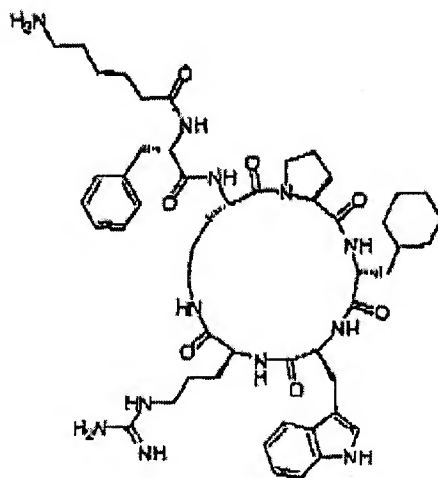
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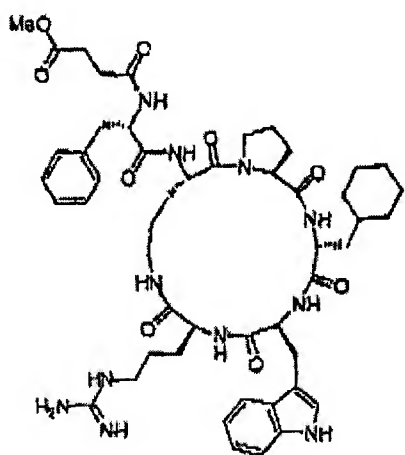
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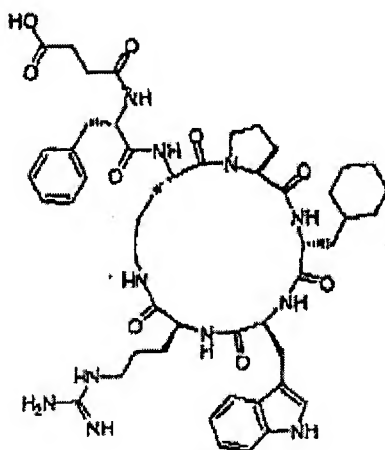
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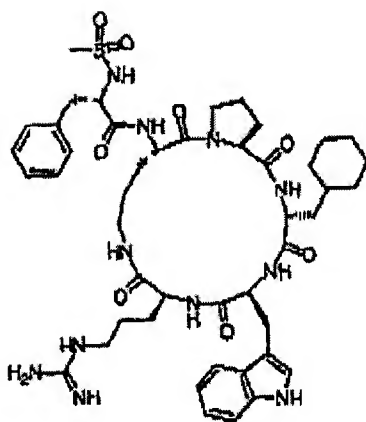
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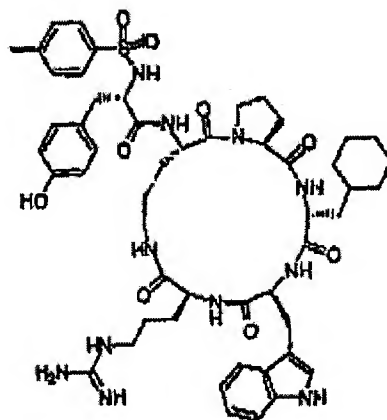
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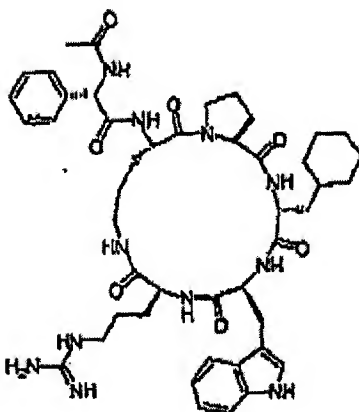
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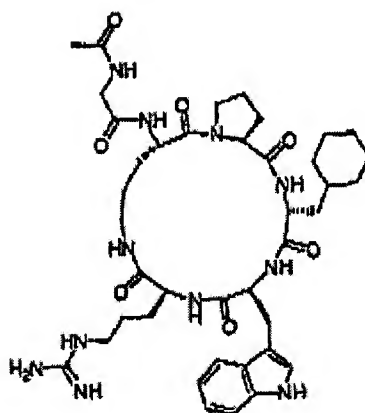
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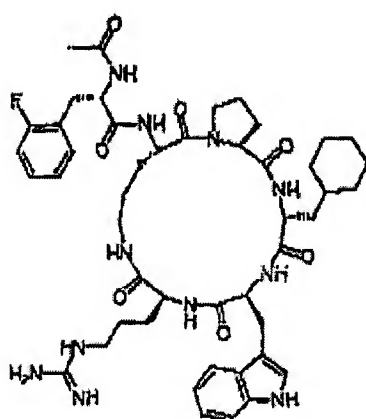
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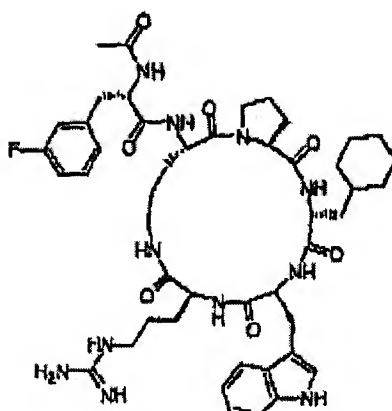
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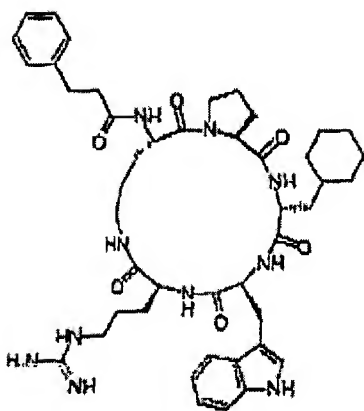
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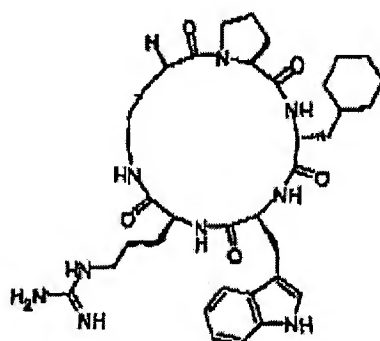
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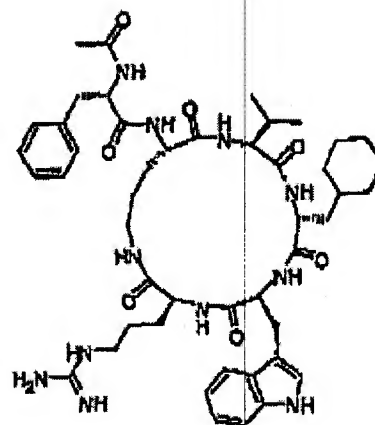
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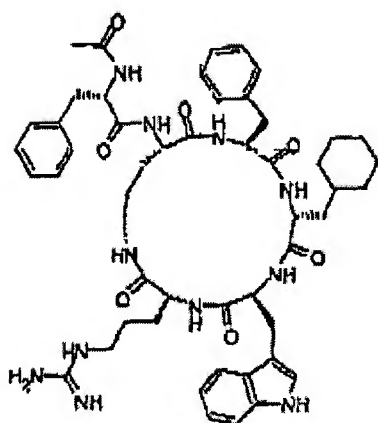
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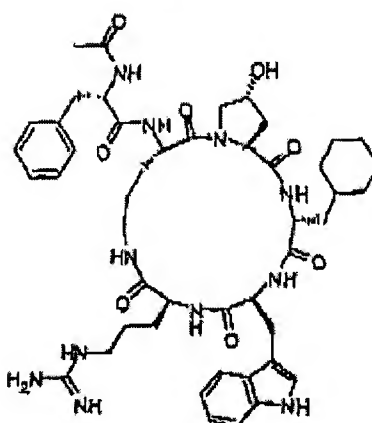
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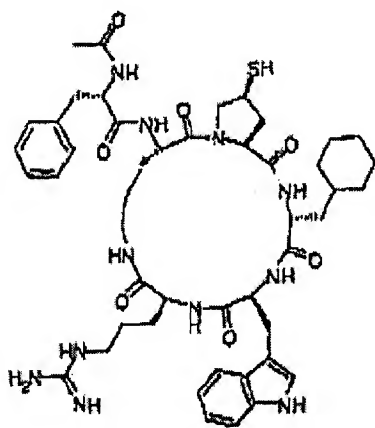
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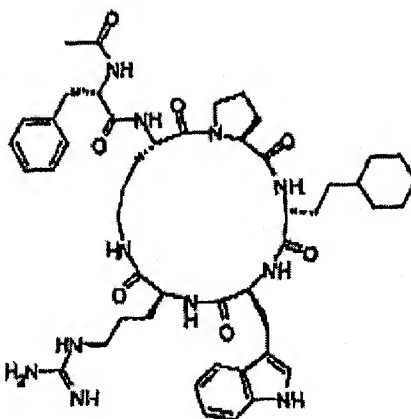
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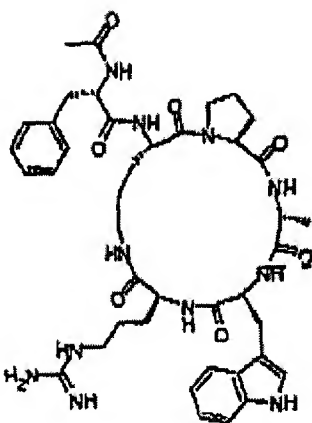
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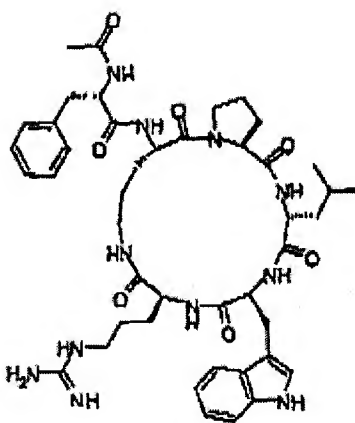
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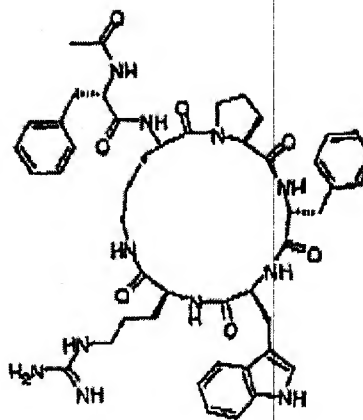
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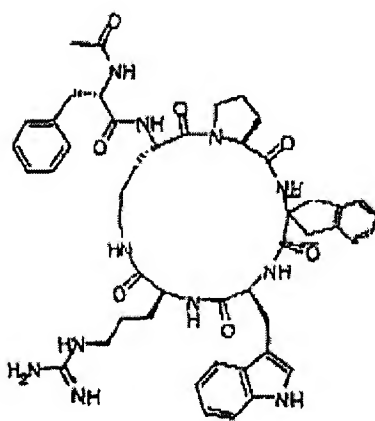
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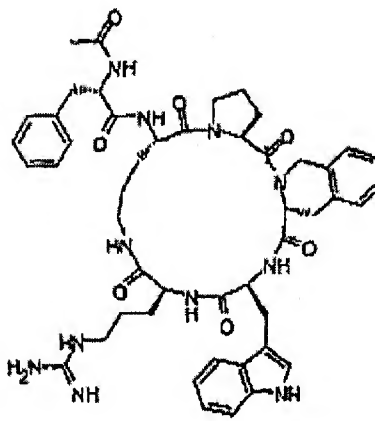
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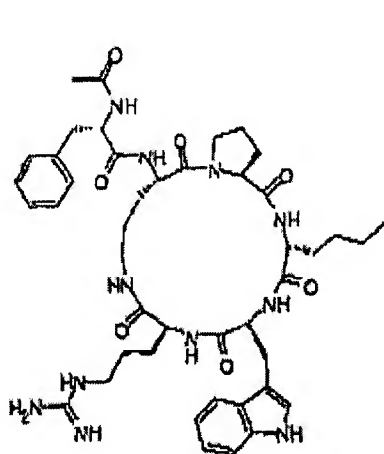
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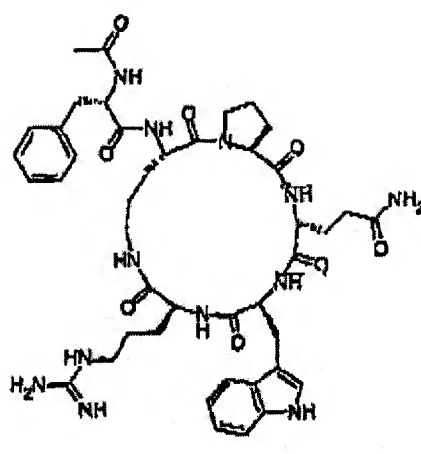
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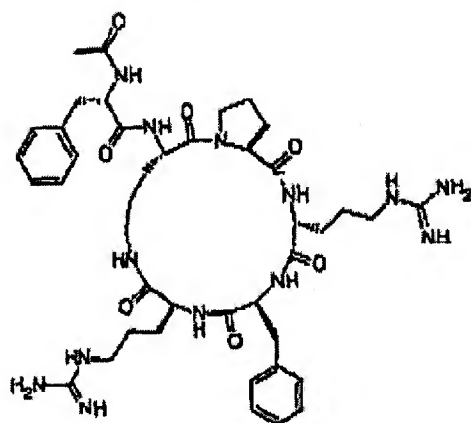
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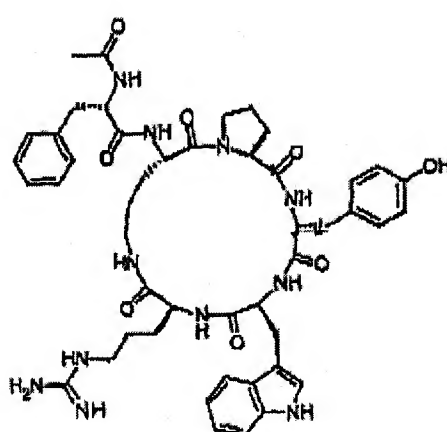
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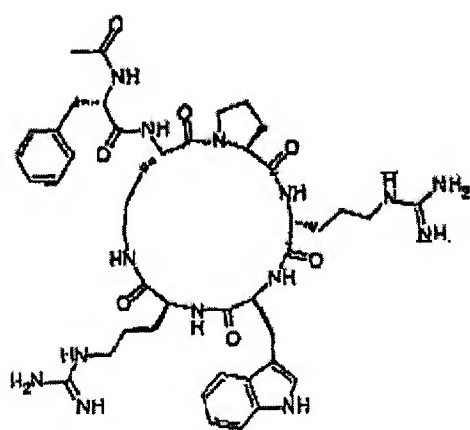
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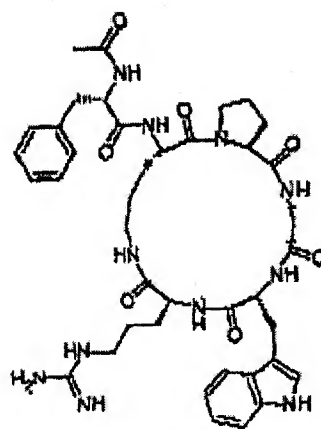
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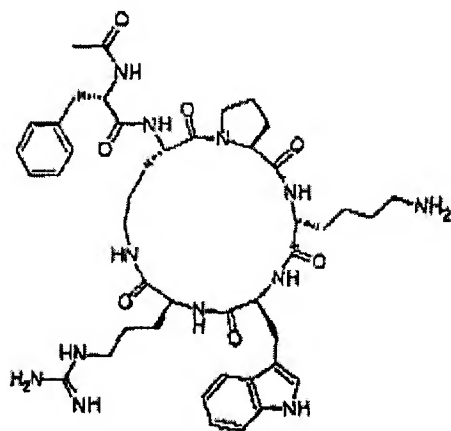
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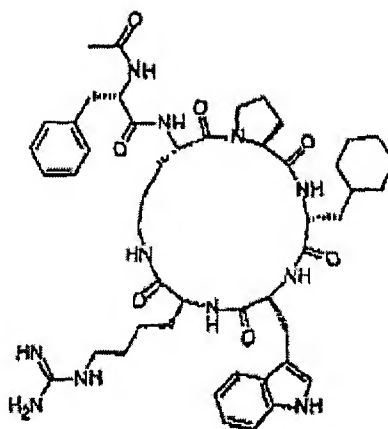
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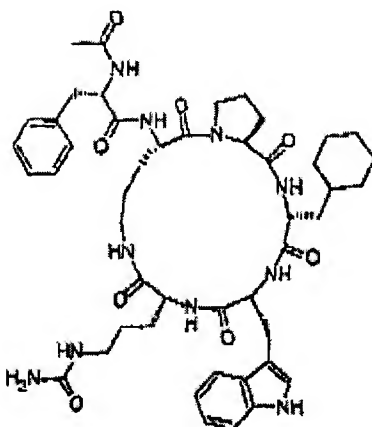
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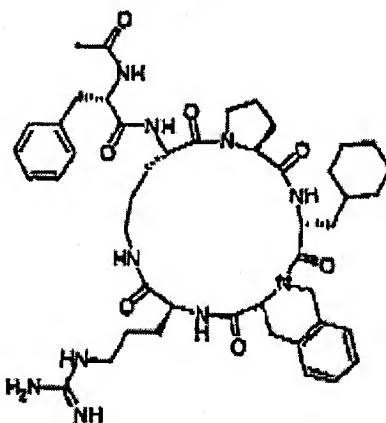
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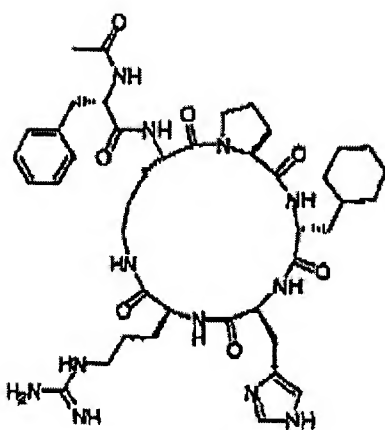
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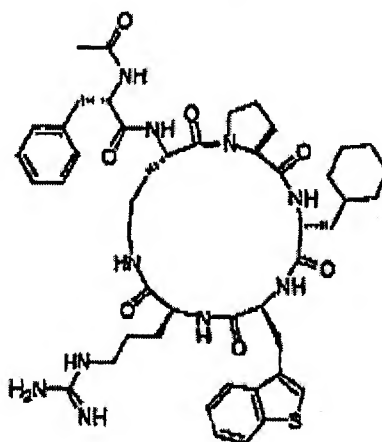
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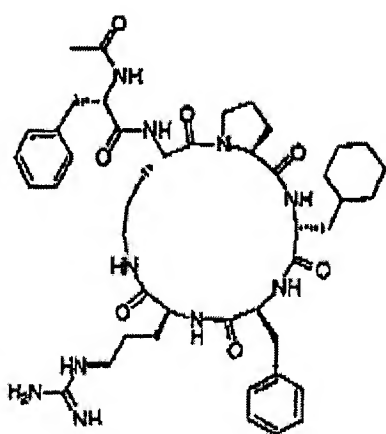
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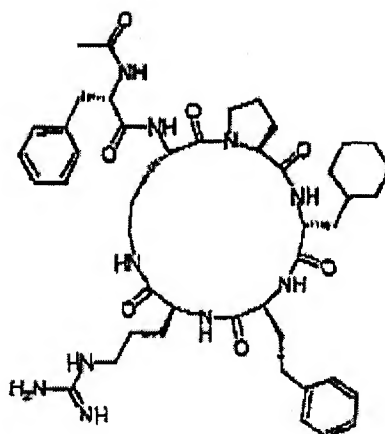
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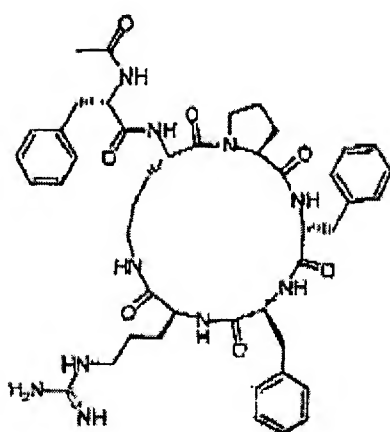
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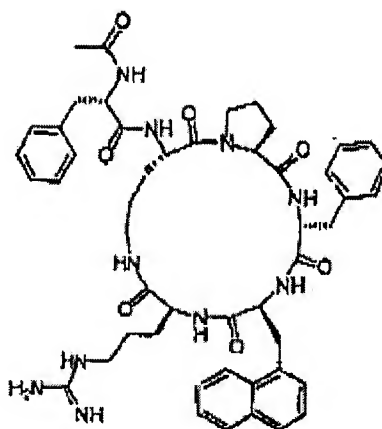
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61

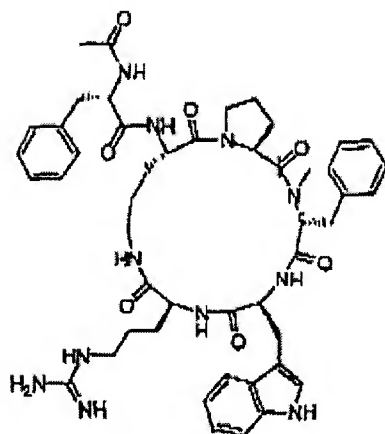


62



63

and

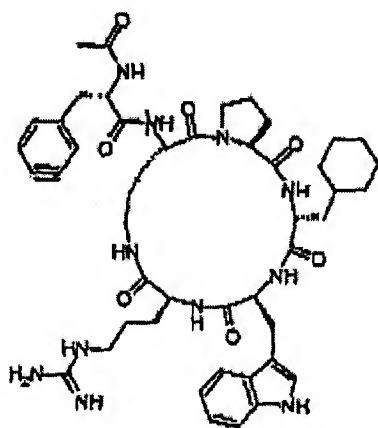


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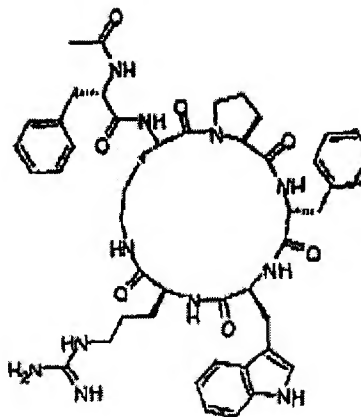
;

wherein said compound is a C5a G protein-coupled receptor antagonist that has substantially no agonist activity.

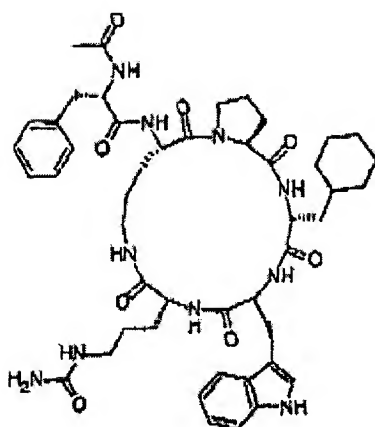
22. (Previously Presented) The method of claim 21, wherein said compound is selected from the group consisting of:



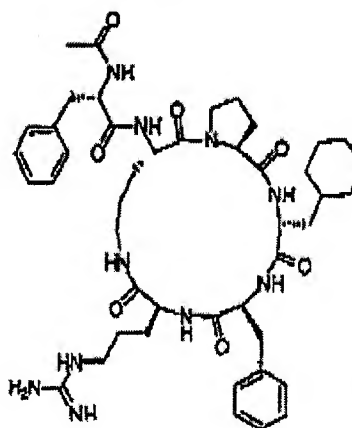
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33



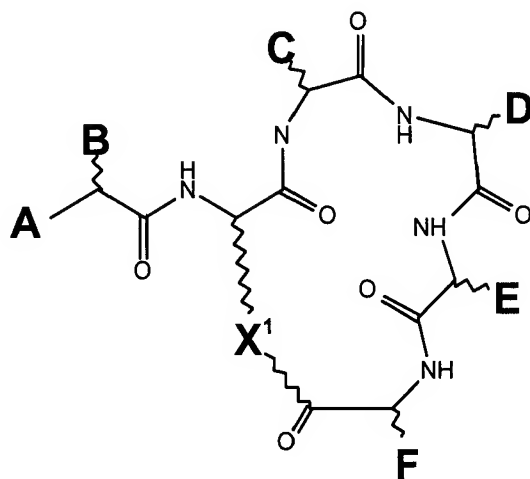
45



60

and

23. (Previously Presented) A method for treating osteoarthritis in a mammal, said method comprising the step of: administering to a mammal in need thereof, an effective amount of a composition comprising a C5a G protein-coupled receptor antagonist compound that (a) has substantially no agonist activity and (b) is a cyclic peptide or peptidomimetic compound of formula I:



(I)

wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and **X¹** is $-(CH_2)_nNH-$, where n is 3.